immunodeficiency. The pneumonias may be primarily viral, bacterial/fungal, or mixed. RSV has been associated with an exceptionally high frequency of the progression to fatal viral pneumonia in some subsets of patients. The mortality of untreated RSV pneumonia in these patients has been > 80%. Studies have suggested that the early initiation of therapy with a combination of aerosolized ribavirin and IVIG may be of benefit. Influenza has been associated with a somewhat lower frequency of progression to fatal viral pneumonia than RSV, however, the spectrum of vulnerable patients has been broader. Because of the large number of immunocompromised patients seriously ill with CRV diseases, effective prophylactic and therapeutic regimens need to be defined expeditiously. This will be a challenge given the diversity of viruses and their widespread prevalence and contagiousness; the limited means of rapid diagnosis; the paucity of prophylactic and therapeutic options; and the wide spectrum of immunocompromised patients with varying vulnerability to serious CRV disease.

S197 Risk assessment and response in suspected imported cases of viral haemorrhagic fevers

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Viral haemorrhagic fevers (VHF) are infrequently seen outside their countries of origin, but cases have occasionally been imported into Europe, the U.S., Oceania, and recently South Africa. During the period of an outbreak in the country of origin, other countries may experience panic, inappropriate responses by officials and others dealing with well and ill immigrants/travellers, delays in diagnosis and treatment of patients with other diseases, and unnecessary laboratory tests, isolation, and surveillance procedures in misclassified suspect cases. Over 95% of suspected imported VHF cases have had a final diagnosis of malaria. On the other hand, unclear or nonexistent policies can also lead to lack of communication between public health personnel, infectious disease physicians, microbiologists, immigration officials, and the public, and to delays in ordering appropriate tests, isolation, treatment, and surveillance of contacts when a VHF should be suspected. Policies should ensure coordinated efforts for prompt recognition of suspected cases leading to appropriate clinical, laboratory, transport, public health, and media responses, but also for prevention of inappropriate suspicion and responses.

Specific guidance has been developed in the U.K. for management and control of VHF, focusing on those that are transmissible person to person. Policy areas include risk assessment, patient management, specimen handling, laboratory procedures, and public health actions. The discussion will focus on this guidance and examples of U.K. coordinated actions to deal with the possibility of imported cases during recent outbreaks of VHF in Africa. It is suggested that countries should consider communication procedures to coordinate the work of clinical personnel with other sectors. It is useful for all hospitals to have policies known to all relevant staff for the management of patients with a pyrexia of unknown origin or a suspected VHF, and procedures for communication with public health officials, specialist clinicians and laboratories, and high security infectious disease units when appropriate. Cases in which a VHF is to be ruled out can be classified by "risk category", and suggested procedures will be discussed for each level of risk. Basic patient information to be collected will be listed, and flow charts for handling of patients and specimens based on risk category will be set out.

Pneumococci: The resistance challenge

S198 Emergence of Internationally-Spread Multidrug-Resistant (MDR) Clones of *Streptococcus pneumoniae*

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I shall discuss three aspects of MDR pneumococci. (i) The *"biological price" of resistance.* Laboratory mutants of pneumococci with the same basic molecular mechanism of penicillin resistance as the one identified in resistant isolates recovered from the clinical environment have a multiplicity of physiological/biochemical defects which are absent from the clinical resistant bugs. New experiments have begun to throw some light on the nature of these extra "fitness" factors present in clinical isolates (but not in laboratory mutants) of resistant pneumococci that allow expression of antibiotic resistance without jeopardizing normal physiology. (ii) *Acquisition and exchange of genetic material* will be illustrated by results documenting the ubiquitous presence of competence (for genetic transformation) genes within the species, and by new experiments documenting *in vivo* exchange of capsular genes in MDR pneumococci. (iii) Properties of 3 internationally-spread MDR clones of *S. pneumoniae* will be summarized including clone-specific properties such as the structure of the resistant PBP genes; unique protein polymorphism of PBPs, unique chromosomal macrorestriction fingerprints and unique cell wall composition. An update on the geographic expansion of these international clones will be provided from prevalence data that include both invasive as well as colonizing isolates.

S199 Genomic Analysis of *Streptococcus pneumoniae*

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Effective therapy for upper-respiratory infections has become compromised in recent years by the emergence of strains that are resistant to commonly used antibiotics such as penicillin. In particular, the wide-spread occurrence of penicillin-resistant *Streptococcus pneumoniae* has become a major concern. To discover new antibiotics that could be used to treat these infections we have initiated a project to identify novel targets in *S. pneumoniae* that are also found in other organisms responsible for upper-respiratory infections such as *Haemophilus influenzae.* Possible targets are being identified by random DNA sequence analysis of the *S. pneumoniae* genome. Sample sequencing has been used to identify genes, which have been mapped to different *Sma*I fragments of the circular chromosome and compared to orthologous genes in other organisms. Internal segments of the genes are being used for insertional mutagenesis to determine if any particular gene is required for viability. An unconventional procedure was developed for these 'knock-out' experiments, which will be described along with the results of the sequence analysis.

S200 The Effect of Antimicrobial Use on the Epidemiology of Penicillin Resistant Pneumococci in Children

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Penicillin resistant and multiresistant pneumococci have spread globally and reached high prevalence rates in many countries. Antimicrobial use is considered to be a major driving force for resistance in

hospitals, but the influence in the community has not been as clearly demonstrated. Only with a clear understanding of all the risk factors involved, can effective control measures be introduced.

The main habitat of the pneumococcus is the nasopharynx of children and antimicrobial use in children is therefore likely to have a significant influence on the susceptibility of pneumococci. Recent studies investigating risk factors for resistance in pneumococci have identified antimicrobial use as a risk factor; especially ongoing, recent, repeated, frequent, and prophylactic use. The effect of individual antimicrobial classes has not been studied in detail, but use of β-lactam antibiotics and sulpha-trimethoprim has been associated with increased risk. Day-care centres can facilitate the spread of resistant pneumococci, and carriage of resistant pneumococci in Iceland was associated with young age, domicile in an area with high antimicrobial consumption, recent antimicrobial use, frequent antimicrobial use and use of trimethoprim-sulpha. Other studies have also shown a correlation between antimicrobial usage in different areas and antimicrobial resistance.

Reduction of antimicrobial use in Iceland, with subsequent reduced incidence of penicillin resistant pneumococci, may indicate a cause and an effect, and should stimulate programs aimed at prudent antimicrobial use.

S201 Treatment Options in Resistant Pneumococcal Infections

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Over the past three decades penicillin-resistant pneumococci have emerged worldwide. In addition, penicillin-resistant strains have also decreased susceptibility to other beta-lactams (including cephalosporins) and these strains are often resistant to other antibiotic groups, making the treatment options much more difficult. Nevertheless, the present in vitro definitions of resistance to penicillin and cephalosporins in pneumococci could not be appropriated for all types of pneumococcal infections. Thus, current levels of resistance to penicillin and cephalosporin seem to have little, if any, clinical relevance in nonmeningeal infections (eg. pneumonia or bacteremia). On the contrary, numerous clinical failures have been reported in patients with pneumococcal meningitis caused by strains with penicillin MIC $\geq$ 0.12 μg/ml, and penicillin should never be used in pneumococcal meningitis except when the strain is known to be fully susceptible to this drug. Nowadays, therapy for pneumococcal meningitis should mainly be selected on the basis of susceptibility to cephalosporins, and most patients may currently be treated with high dose cefotaxime ($\pm$) vancomycin, depending on the levels of resistance in the patient's geographic area. However, it should be emphasized that the most appropriate antibiotic therapy for infections caused by resistant pneumococci remains controversial, and comparative, randomized studies are urgently needed in order to clarify the best antibiotic therapy for these infections. We will present a practical approach, based on current levels of antibiotic resistance, for treating the most prevalent pneumococcal infections.

S202 Global epidemiology of the PBP2x gene of penicillin-resistant pneumococci

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Penicillin-binding proteins (PBPs) functioning as selectable resistance determinants can be used to investigate the number of species contributing to a gene pool that is accessible for a pathogen such as *Streptococcus pneumoniae*. PBP2x is one of the primary penicillin resistance determinants in *S. pneumoniae*, and all penicillin-resistant isolates contain mosaic *pbp2x* genes where parts are replaced by homologous sequences from related species. Mosaic homologues of *pbp2x* are present in penicillin sensitive *S. mitis* and *S. oralis*, demonstrating that transfer of *pbp2x* sequences has occurred independent on resistance to penicillin. Transfer of *pbp2x* genes between susceptible species could indeed be observed under laboratory conditions. One class of *pbp2x* with a high degree of similarity to the *S. oralis pbp2x* were found in resistant strains of different biovars of *S.mitis* and *S. oralis*, and major clones of *S. pneumoniae* from different countries and even continents. Sequence comparison documents that at least another two species participate in the genetic exchange of resistance determinants. The data obtained raise the question on the definition of species-specific sequences for selectable markers in naturally transformable bacteria.

Prevention strategies for Health-Care Workers (Joint Symposium with the Centers for Disease Control and Prevention, Atlanta, USA)

S203 Bloodborne Pathogens: Update on post-exposure management and prophylaxis

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In 1996, the U.S. Public Health Service recommended post-exposure prophylaxis (PEP) after certain occupational HIV exposures (MMWR 1996); 45: 468–72). This recommendation was based in part on a case-control study of health-care workers exposed to HIV in the USA and Europe in which zidovudine PEP was associated with an approximately 80% reduction in risk of seroconversion (MMWR 1995; 44: 929–33). CDC has received many inquiries, e.g., concerning implementation, use of newly licensed drugs for PEP, and possible use of PEP for sexual exposures. Periodic updates are expected; a major difficulty is limited data on toxicity and efficacy of PEP.

For hepatitis C virus (HIV), no PEP is available. Evaluation of workers with percutaneous or mucosal exposure to blood from source patients positive for anti-HCV might include 6-month follow-up testing of the exposed worker for anti-HCV and serum alanine amino transferase (ALT) activity. All repeatedly reactive tests by EIA should be confirmed by supplemental anti-HCV testing.

S204 The pregnant health-care worker: are special precautions necessary?

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Immunologic changes that occur during pregnancy generally do not increase susceptibility to infectious diseases. Nevertheless, nosocomial transmission of certain infections may be of particular concern to pregnant health-care workers for a variety of reasons. Some infections, such as varicella, may be more severe during pregnancy.

Transplacental infection with viruses such as parvovirus, varicella, and rubella has been associated with abortion, congenital anomaly, and/or mental retardation. Finally, certain drugs used to treat or prevent some infections, e.g., tuberculosis, may be contraindicated during pregnancy. Pre-employment screening followed by appropriate immunizations can prevent many infections in health-care workers, pregnant or not. Further, careful adherence to infection control practices should minimize occupational exposures and nosocomial infections in pregnant health-care workers.